U.S. Patent Application Serial No. 10/593,911 Response to November 13, 2009 Office Action Page 2 of 22

## Claim Amendments.

1. (currently amended): A compound of formula I:

or a pharmaceutically acceptable derivative thereof, wherein:

ring A is optionally substituted and is a heteroaryl selected from

each R<sup>1</sup> and R<sup>2</sup> is independently H, alkyl, or fluoroalkyl;

R<sup>3</sup> is H, alkyl, fluoroalkyl, aralkyl, carbocyclylalkyl, heterocyclyl, carbocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroaralkyl, -C(O)R, -OR,

-(CH<sub>2</sub>)<sub>1-6</sub>OR, -(CH<sub>2</sub>)<sub>1-6</sub>N(R)<sub>2</sub>, -N(R)<sub>2</sub>, or -C(H)(OR)R;

R<sup>4</sup> is H, alkyl, fluoroalkyl, -CO<sub>2</sub>R, -CON(R)<sub>2</sub>, carbocyclyl, carbocyclylalkyl, heteroaryl, or heterocyclyl;

 $R^5$  is  $-OR^7$  or  $-NR^8R^9$ ;

R<sup>6</sup> is -C(O)R, -C(S)R, -C=C-C(O)R, -SR, -S-W-OR<sup>7</sup>, M, or Y;

$$R^1$$
 $R^2$ 
 $R^3$ 
 $R^4$ 
 $R^3$ 
 $R^5$ 
 $R^5$ 
 $R^5$ 

Attorney Docket No.: A33-013US

 $R^7 \text{ is } R^\circ, -C(O)R, -C(O)N(R)_2, -C(O)OR, -(CH_2)_{1-6}-C(O)R, -PO_3M_x, \\ -P(O)(alkyl)OM', -(PO_3)_2M_y, \text{ carbocyclyl, aryl, heterocyclyl, heteroaryl,} \\ \text{carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety;} \\$ 

x is 1 or 2;

y is 1, 2 or 3;

each M is independently H, Li, Na, K, Mg, Ca, Mn, Co, Ni, Zn, or alkyl;

M' is H, Li, Na, K, or alkyl;

R<sup>8</sup> is H or alkyl;

 $R^9$  is H, alkyl, -C(O)R,  $-C(O)N(R)_2$ , -C(O)OR,  $-SO_2R$ ,  $-SO_2N(R)_2$ , carbocyclyl, aryl, heterocyclyl, heterocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor targeting moiety;

each R<sup>a</sup> and R<sup>b</sup> is independently H, OR°, alkyl, or fluoroalkyl;

each R<sup>c</sup> and R<sup>d</sup> is independently H, alkyl, or fluoroalkyl;

n is 0-4;

W is alkylene, arylene, heteroarylene, carbocyclylene, or heterocyclylene;

R° is H or alkyl; and

R is  $R^{\circ}$ , carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, or heteroaralkyl.

- 2. (currently amended) The compound of claim 1, wherein R<sup>6</sup> is Y or -SR.
- 3. (cancelled).

U.S. Patent Application Serial No. 10/593,911 Response to November 13, 2009 Office Action Page 4 of 22

- 4. (previously amended) The compound of claim 1, wherein:
  - i)  $R^1$ ,  $R^2$  and  $R^4$  are independently H,  $C_{1-6}$  alkyl or fluoro( $C_{1-6}$  alkyl);
  - ii)  $R^3$  is H, alkyl, fluoroalkyl,  $-(CH_2)_{1-6}OR$ ,  $-(CH_2)_{1-6}N(R)_2$ ,
- $-NR^{\circ}C(O)R$ , -C(O)R, -C(H)(OR)R, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl;
  - iii)  $R^6$  is -C=C-C(O)R, -SR, -S-W-OR<sup>7</sup>, M or Y;
- iv)  $R^7$  is H, alkyl, -C(O)R,  $-PO_3M_x$ ,  $-(PO_3)_2M_y$ , -P(O)(alkyl)OM',  $-C(O)N(R)_2$ , -C(O)OR, or a tumor-targeting moiety; or  $R^9$  is H, alkyl, -C(O)R,  $-C(O)N(R)_2$ , -C(O)OR,  $-SO_2R$ , 5-membered heterocyclyl, 5-membered heteroaralkyl, or a tumor-targeting moiety; and
  - v) n is 1.
- 5. (previously amended) The compound of claim 4, wherein R is R<sup>o</sup>, carbocyclyl, aryl, heteroaryl, heterocyclyl, aralkyl, heterocyclylalkyl or heteroaralkyl.
- 6. (previously amended) The compound of claim 5, wherein  $R^{\circ}$  is H or  $C_{1-6}$  alkyl optionally substituted with halo, hydroxy or amino.
- 7. (currently amended) The compound of claim 4, wherein said compound has one or more of the features selected from the group consisting of:
- i) ring A is optionally substituted with  $-NH_2$ , alkyl,  $-OC(O)R^{\dagger}$ , halo,  $-OR^{\dagger}$ ,  $-CF_3$ ,  $-OCF_3$ ,  $-SCF_3$ ,  $-SR^{\dagger}$ ,  $-R^{\dagger}$ ,  $-NR^{\dagger}C(O)R^{\dagger}$ ,  $-CO_2R^{\dagger}$ ,  $-NO_2$ ,  $-N(R^{\dagger})_2$ , -CN,  $-C(O)R^{\dagger}$ ,  $-C(O)N(R^{\dagger})_2$ ,  $-SO_2N(R^{\dagger})_2$ ,  $-NR^{\dagger}CO_2R^{\dagger}$ ,  $-C(O)C(O)R^{\dagger}$ ,  $-OC(O)N(R^{\dagger})_2$ ,  $-S(O)_tR^{\dagger}$ ,  $-C(O)CH_2C(O)R^{\dagger}$ ,  $-NR^{\dagger}SO_2R^{\dagger}$ , or  $-C(=S)N(R^{\dagger})_2$ ; and  $R^{\dagger}$  is 3-6 membered unsubstituted cycloalkyl, phenyl, benzyl, naphthyl, pyridyl, or  $C_{1-6}$  alkyl optionally substituted with halo;
  - ii)  $R^3$  is H,  $C_{1-6}$  alkyl,  $-(CH_2)_{1-6}OR^o$  or  $-CH(OR^o)R^o$ ;

- Attorney Docket No.: A33-013US
- iii)  $R^6$  is -C=C-C(O)R, -SR, -S-W-OR<sup>7</sup> or Y; and
- iv) R<sup>8</sup> is H or C<sub>1-6</sub> unsubstituted alkyl.
- 8. (currently amended) The compound of claim 7, wherein  $R^7$  or  $R^9$  is  $\underline{H}$ , a polysaccharide,  $-[C(O)CH(R)N(R)]_{2-3}-R$ , an antibody, or

$$\stackrel{\text{d}}{\sim} \stackrel{\text{o}}{\sim} \stackrel{\text{o}}{\sim} \stackrel{\text{o}}{\sim} \text{,wherein R}^{10} \text{ is H, alkyl, or aryl.}$$

- 9. (currently amended) The compound of claim 7, wherein said compound has one or more of the features selected from the group consisting of:
  - i) ring A is selected from the group consisting of <u>1-9</u>;
  - ii) R<sup>1</sup>, R<sup>2</sup> and R<sup>4</sup> are independently H, methyl, ethyl, -CH<sub>2</sub>F, -CHF<sub>2</sub>, or -CF<sub>3</sub>;
  - iii) R<sup>3</sup> is H, methyl, ethyl, -CH(OH)CH<sub>3</sub>, -CH<sub>2</sub>OH, or -CH<sub>2</sub>CH<sub>2</sub>OH;
  - iv iii)  $R^6$  is <u>-S-( heterocyclylalkyl)</u>, ( -S-(unsubstituted  $C_{1-6}$  alkyl), Y,

$$H_3C$$
  $O$   $O$   $CH_3$  ;

- $\underline{i}v$ )  $R^8$  is H, methyl, or ethyl; and
- vi)  $R^7$  is H, methyl, ethyl, -C(O)Me, -C(O)Et,  $-C(O)NMe_2$ , -C(O)-p-OMephenyl, -C(O)O-phenyl,  $-PO_3H_2$ ,  $-P(O)(OMe)_2$ , -P(O)(OMe)OH, -P(O)(Me)OH, -P(O)(OH)OP(O)(OH)(OH), or  $R^{11}$ ; and  $R^{11}$  is selected from the group consisting of:

Attorney Docket No.: A33-013US

R<sup>9</sup> is H, methyl, ethyl, R<sup>11</sup>,

U.S. Patent Application Serial No. 10/593,911 Response to November 13, 2009 Office Action Page 8 of 22

10. (currently amended) The compound of claim1, wherein said compound is selected from the group consisting of the compounds of: (1) formula **IIa** 

$$\mathbb{R}^{\frac{N}{1}}$$
  $\mathbb{R}^{4}$   $\mathbb{R}^{3}$   $\mathbb{R}^{6}$   $\mathbb{R}^{6}$   $\mathbb{R}^{7}$   $\mathbb{R}^{3}$   $\mathbb{R}^{6}$ 

where R<sup>3</sup> and R<sup>4</sup> are independently H or alkyl, R<sup>6</sup> is -SR, R<sup>7</sup> is R°, and R<sup>x</sup> can be the same or different and is selected from the group consisting of alkyl and NH<sub>2</sub> (2) formulae III-1 13 to III-18, and or (3) formulae IV-1 13 to IV-18.

- 11. (previously amended) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
- 12.-22. (cancelled).

U.S. Patent Application Serial No. 10/593,911 Response to November 13, 2009 Office Action Page 9 of 22

## 23. (new) A compound of the formula:

$$\begin{array}{c} \text{H}_{2}\text{N} \\ \text{N} \\ \text{OH} \end{array}$$

$$\begin{array}{c} \text{NH}_2 \\ \text{NH}_2 \\$$

(d)

(f)

(g)

(h)

(i)

(j)

(k)

(l)

Page 14 of 22

(m)

(n)

(o)

U.S. Patent Application Serial No. 10/593,911 Response to November 13, 2009 Office Action Page 16 of 22

(p)

or a pharmaceutically acceptable derivative thereof.

24. (new) The compound of claim 23, wherein the compound is:

U.S. Patent Application Serial No. 10/593,911 Response to November 13, 2009 Office Action Page 17 of 22

## 25. (new) A compound of the formula

$$\begin{pmatrix}
R^{3} \\
 & R^{4}
\end{pmatrix}$$

$$\begin{pmatrix}
R^{3} \\
 & R^{4}
\end{pmatrix}$$

$$\begin{pmatrix}
R^{3} \\
 & R^{6}
\end{pmatrix}$$

$$\begin{pmatrix}
R^{7} \\
 & R^{7}
\end{pmatrix}$$

or a pharmaceutically acceptable derivative thereof, wherein:

- (a) R<sup>3</sup> and R<sup>4</sup> may each be the same or different to the extent they occur more than once in the compound and are independently H or alkyl;
- (b) R<sup>7</sup> may be the same or different to the extent it occurs more than once in the compound and is independently R° or -C(O)R, where R° is H or alkyl and R is R°, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, or heteroaralkyl;
- (c) R<sup>x</sup> may be the same or different to the extent it occurs more than once in the compound and is independently alkyl or NH<sub>2</sub>;

(d) 
$$R^6$$
 is  $-SR$ ,  $-C(O)R$ ,

or

; and

(e) n is 0, 1, 2, or 3.